~~APPROVED PA~~DRAFT PA Criteria

Initial Approval Date: July 11, 2018
Revised Dates: July 8, 2020; January 8, 2020;
October 9, 2019; January 20, 2021

CRITERIA FOR PRIOR AUTHORIZATION

Multiple Sclerosis (MS) Agents

BILLING CODE TYPE For drug coverage and provider type information, see the KMAP Reference Codes webpage.

MANUAL GUIDELINES: Prior authorization will be required for all current and future dose forms available. All medication-specific criteria, including drug-specific indication, age, and dose for each agent is defined in Table 1 below.

GENERAL CRITERIA FOR INITIAL PRIOR AUTHORIZATION: (must meet all of the following)

- Must be approved for the indication, age, and not exceed dosing limits listed in Table 1. Refer to Table 3 for definitions of types of disease.
- Medication must be prescribed by or in consultation with a neurologist.
- For all agents listed, the preferred PDL drug, if applicable, which treats the PA indication, is required unless the patient meets the non-preferred PDL PA criteria.
- Patient must not be on concurrent therapy with another disease modifying MS agent listed in Table 2.
- For Vumerity® and Bafiertam® (must meet all of the following):
  - Patient must have had an adequate trial (at least 90 consecutive days) of dimethyl fumarate (generic Tecfidera®).
  - Prescriber must provide a compelling rationale of why the patient will benefit from Vumerity® or Bafiertam® over dimethyl fumarate (generic Tecfidera®). Gastrointestinal side effects are not accepted as rationale.

Table 1. FDA-approved age and dosing limits for Multiple Sclerosis (MS) Agents.[3-21]

Agents	Indication(s)	Age	Dosing Limits
Anti-CD20 Monoclonal Antibodies			
Ocrelizumab (Ocrevus®)	PPMS, CIS, RRMS, SPMS	≥ 18 years	300 mg IV on day 1, followed by 300 mg IV 2 weeks later, subsequent doses of 600 mg IV are administered once every 6 months (beginning 6 months after the first 300 mg dose)
Ofatumumab (Kesimpta®)	CIS, RRMS, SPMS	≥ 18 years	20 mg SC week 0, 1 and 2, then 20 mg SC monthly starting at week 4
Anti-CD52 Monoclonal Antibodies			
Alemtuzumab (Lemtrada®)	RRMS, SPMS	≥ 18 years	12 mg/day IV on 5 consecutive days (total 60 mg) followed 12 months later by 12 mg IV daily for 3 consecutive days (total 36 mg)
Fumaric Acid Derivatives			
Dimethyl Fumarate (Tecfidera®)	CIS, RRMS, SPMS	≥ 18 years	240 mg orally twice daily
Diroximel Fumarate (Vumerity®)	CIS, RRMS, SPMS	≥ 18 years	462 mg orally twice daily
Monomethyl Fumarate (Bafiertam®)	CIS, RRMS, SPMS	≥ 18 years	190 mg orally twice daily
Interferons			

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Agents	Indication(s)	Age	Dosing Limits
Interferon Beta-1a (Avonex®)	CIS, RRMS, SPMS	≥ 18 years	30 mcg IM once per week
Interferon Beta-1a (Rebif®)	CIS, RRMS, SPMS	≥ 18 years	44 mcg SC 3 times per week
Interferon Beta-1b (Betaseron®, Extavia®)	CIS, RRMS, SPMS	≥ 18 years	0.25 mg SC every other day
Peginterferon Beta-1a (Plegridy®)	CIS, RRMS, SPMS	≥ 18 years	63 mcg SC on day 1, 94 mcg SC on day 15, then 125 mcg SC on day 29 and every 14 days thereafter
Miscellaneous Biologic Immunosuppressants			
Glatiramer (Copaxone®, Glatopa®)	CIS, RRMS, SPMS	≥ 18 years	20 mg SC once daily or 40 mg SC 3 times per week
Purine Analog Antimetabolites			
Cladribine (Mavenclad®)	RRMS, SPMS	≥ 18 years	3.5 mg/kg orally over a 2-year treatment course, administered as 1.75 mg/kg in each year, no more than 20 mg per day
Pyrimidine Synthesis Inhibitors			
Teriflunomide (Aubagio®)	CIS, RRMS, SPMS	≥ 18 years	14 mg orally once daily
Selective Adhesion-Molecule Inhibitors			
Natalizumab (Tysabri®)	CIS, RRMS, SPMS	≥ 18 years	300 mg IV infusion every 4 weeks
Sphingosine 1-Phosphate (S1P) Receptor Modulator			
Fingolimod (Gilenya®)	CIS, RRMS, SPMS	≥ 10 years	Adults: 0.5 mg orally once daily Pediatric: ≥10 years of age and ≤40 kg: 0.25 mg orally once daily ≥10 years of age and >40 kg: 0.5 mg orally once daily
Ozanimod (Zeposia®)	CIS, RRMS, SPMS	≥ 18 years	0.92 mg orally once daily
Siponimod (Mayzent®)	CIS, RRMS, SPMS	≥ 18 years	CYP2C9 Genotype *1/*1, *1/*2, or *2/*2: 0.25 mg orally once daily on Days 1 and 2, then 0.5 mg once daily on Day 3, then 0.75 mg once daily on Day 4, then 1.25 mg once daily on Day 5, then 2 mg once daily, beginning on Day 6 CYP2C9 Genotype *1/*3 or *2/*3: 0.25 mg orally once daily on Days 1 and 2, then 0.5 mg once daily on Day 3, then 0.75 mg once daily on Day 4, then 1 mg once daily, beginning on Day 5

IV: intravenously. SC: subcutaneously. IM: intramuscularly. CIS: clinically isolated syndrome. RRMS: relapsing-remitting multiple sclerosis. SPMS: secondary progressive multiple sclerosis. PPMS: primary progressive multiple sclerosis.

CRITERIA FOR RENEWAL PRIOR AUTHORIZATION: (must meet all of the following)

- Prescriber must attest that the patient has received clinical benefit from continuous treatment with the requested medication.[2]
- Must not exceed dosing limits listed in Table 1.
- Patient must not be on concurrent therapy with another disease modifying MS agent listed in Table 2.

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- For Lemtrada (alemtuzumab): therapy does not exceed 2 total treatments (5 consecutive days of injections in the first year and 3 consecutive days of injections in the second year)

LENGTH OF APPROVAL (INITIAL AND RENEWAL): 12 months

FOR DRUGS THAT HAVE A CURRENT PA REQUIREMENT, BUT NOT FOR THE NEWLY APPROVED INDICATIONS, FOR OTHER FDA-APPROVED INDICATIONS, AND FOR CHANGES TO AGE REQUIREMENTS NOT LISTED WITHIN THE PA CRITERIA:

- **THE PA REQUEST WILL BE REVIEWED BASED UPON THE FOLLOWING PACKAGE INSERT INFORMATION: INDICATION, AGE, DOSE, AND ANY PRE-REQUISITE TREATMENT REQUIREMENTS FOR THAT INDICATION.**

LENGTH OF APPROVAL (INITIAL AND RENEWAL): 12 months

Table 2. List of disease-modifying therapies (DMTs) (agents not to be used concurrently)

Disease-Modifying Therapies (DMTs)		
Aubagio® (teriflunomide)	Gilenya® (fingolimod)	Plegridy® (interferon beta-1a)
Avonex® (interferon beta-1a)	Glatopa® (glatiramer)	Rebif® (interferon beta-1a)
Bafiertam™ (monomethyl fumarate)	Kesimpta® (ofatumumab)	Tecfidera® (dimethyl fumarate)
Betaseron® (interferon beta-1b)	Lemtrada® (alemtuzumab)	Tysabri® (natalizumab)
Copaxone® (glatiramer)	Mitoxantrone	Vumerity® (diroximel fumarate)
Extavia® (interferon beta-1b)	Ocrevus® (ocrelizumab)	Zeposia® (ozanimod)

Table 3: Definitions of types of MS[1]

Clinically Isolated Syndrome (CIS)	First clinical episode that is suggestive of MS. no evidence of previous episodes of demyelination from the patient's history.
Relapsing-remitting MS (RRMS)	Clearly defined attacks (also known as relapses or exacerbations) with full or incomplete recovery. There is minimal disease progression during the periods between disease relapses, at least as traditionally understood, though relapses themselves may leave severe residual disability.
Active secondary progressive MS (SPMS)	An initial relapsing-remitting MS disease course followed by gradual worsening with or without occasional relapses, minor remissions, and plateaus. The transition from relapsing-remitting MS to secondary progressive MS usually occurs 10 to 20 years after disease onset. Active disease is characterized with relapses and/or evidence of new MRI activity.
Primary progressive MS (PPMS)	Relatively steady progression of symptoms over time. Progressive accumulation of disability from disease onset with occasional plateaus, temporary minor improvements, or acute relapses still consistent with the definition. The most common clinical presentation is a spinal cord syndrome that worsens over months or years with asymmetric spastic paraparesis and no clear sensory level.

Notes:

Lemtrada (alemtuzumab)	Generally reserved for patients who have had an inadequate response to 2 or more medications indicated for the treatment of MS. Subsequent treatment courses of 12 mg IV daily for 3 consecutive days (total 36 mg) may be administered if necessary; courses should be administered no earlier than 12 months after the last dose of the prior treatment cycle.
Mavenclad (cladribine)	Dosing is 3.5 mg/kg over 2-year treatment course, administered as 1.75 mg/kg in each year. Divide the 1.75 mg/kg dose over 2 cycles, each cycle lasting 4 to 5 consecutive days. In the first-year treatment course, initiate the first cycle at any time; administer the second cycle 23 to 27 days after the last dose of the first cycle. In the second-year treatment course, initiate the first cycle ≥43 weeks after the last dose of the first year's second cycle. Administer the second cycle 23 to 27 days after the last dose of the second year's first cycle. Following 2 years of treatment, do not administer oral cladribine during the next 2 years. Maximum dose: 3.5 mg/kg over 2 years; 20 mg/day.
Zinbryta (daclizumab)	Voluntarily withdrawn from the market in 2018.

References:

1. Costello, K., et al. The use of disease-modifying therapies in multiple sclerosis: principles and current evidence. A consensus paper by the multiple sclerosis coalition (2019). Available at https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/DMT_Consensus_MS_Coalition.pdf. Accessed 9/5/19.
2. Rae-Grant, A., Day G et al. Marrie. Practice guideline: disease-modifying therapies for adults with multiple sclerosis. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Full version available at https://www.aan.com/Guidelines/Home/GuidelineDetail/899. Accessed 9/5/19. Abridged version available at Neurology 2018;90(17):777-88.
3. Ocrevus (ocrelizumab) [prescribing information]. South San Francisco, CA: ~~Genetech~~Genentech Inc; November 2020.
4. Lemtrada (alemtuzumab) [prescribing information]. Cambridge, MA: Genzyme Corporation; September 2020.
5. Tecfidera (dimethyl fumarate) [prescribing information]. Cambridge, MA: Biogen Idec Inc; February 2020.
6. Avonex (interferon beta-1a) [prescribing information]. Cambridge, MA: Biogen Idec Inc; March 2020.
7. Rebif (interferon beta-1a) [prescribing information]. Rockland, MA: EMD Serono Inc; October 2020.
8. Betaseron (interferon beta-1b) [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; October 2020.
9. Extavia (interferon beta-1b) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2020.
10. Plegridy (peginterferon beta-1a) [prescribing information]. Cambridge, MA: Biogen Idec Inc; March 2020.
11. Copaxone (glatiramer acetate) [prescribing information]. North Wales, PA: Teva Pharmaceuticals; July 2020.
12. Glatopa (glatiramer acetate) [prescribing information]. Princeton, NJ: Sandoz Inc; July 2020.

13. Mavenclad (cladribine tablets) [prescribing information]. Rockland, MA: EMD Serono Inc; April 2019.
14. Aubagio (teriflunomide) [prescribing information]. Cambridge, MA: Genzyme Corporation; November 2020.
15. Tysabri (natalizumab) [prescribing information]. Cambridge, MA: Biogen Inc; June 2020.
16. Gilenya (fingolimod) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2019.
17. Mayzent (siponimod) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020.
18. Vumerity (diroximel fumarate) [prescribing information]. Cambridge, MA: Biogen Inc; August 2020.
19. Bafiertam (monomethyl fumarate) [prescribing information]. High Point, NC: Banner Life Sciences LLC; April 2020.
20. Zeposia (ozanimod) [prescribing information]. Summit, NJ: Celgene Corporation; September 2020.
~~20.~~21. Kesimpta (ofatumumab) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2020.

DRUG UTILIZATION REVIEW COMMITTEE CHAIR	PHARMACY PROGRAM MANAGER DIVISION OF HEALTH CARE FINANCE KANSAS DEPARTMENT OF HEALTH AND ENVIRONMENT
DATE	DATE